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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,320	03/12/2004	Akira Saikawa	074129-0546	8190

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EXAMINER	
EBERHARD, JEFFREY S	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/799,320	SAIKAWA ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Eberhard, Ph.D.	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-20 and 24-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *:/03122004, 02142005/.*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on January 16, 1998. It is noted, however, that the applicant has not filed a certified copy of the English translation of Japanese Application 10-6412 as required by 35 U.S.C. 119(b).

Specification Objections

2. The disclosure is objected to because of the following informalities:

The substitute specification filed March 12, 2004 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: the amendments are presented in a separate document as an addendum to the original specification. The number and nature of the amendments render it difficult to consider the application, and to arrange the paper for printing and copying. Rewrite the specification to consist of a single document with amended text clearly annotated as such, and readily differentiated from text of the original version.

Reference numbering in the amendments to the specification is not completely consistent with the reference numbering in the originally submitted version of the specification. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 24, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 reads "a method of suppressing bioactive substance initial burst..." None of the embodiments taught in the application specifically define "suppression" in this context, and there is no means taught for assessing said suppression. Therefore, the claim is rejected for failure to establish criteria for assessing the extent of suppression of "bioactive initial burst..." in one particular embodiment over another.

Claim 25 reads "a method of increasing the efficiency of bioactive substance..." None of the embodiments taught in the application specifically define "increasing efficiency" in this context, and there is no means taught for assessing said increase. Therefore, the claim is rejected for failure to establish criteria for assessing improved efficiency of "a method of increasing the efficiency of bioactive substance..." in one particular embodiment over another.

Claim 26 lacks a transitional phrase such as "consisting of," "comprising," "consisting essentially of" or "having" to clarify the scope of a claim when joined with the preamble and body of the claim. Specifically, said phrases in proper context place limits on any unrecited additional components or steps that might be read into a claim. Lacking said transitional phrase the claim is rendered indefinite.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 - 20, 24, 25 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for examples disclosed therein (p. 42, l. 25 – p. 46, l. 20), does not reasonably provide enablement for the breadth of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures made in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986, and again in *In Re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and include nature and scope of the invention, state of the art and level of artisan's skill, guidance and examples provided by the applicant, level of predictability, and amount of experimentation.

The nature of the invention is the formulation and use of a dosage form comprising a biologically active substance, a biodegradable polymer and hydroxynaphthoic acid. Said dosage form is claimed to have sustained release properties specifically related to addition of the hydroxynaphthoate stabilizing agent supplementing or modifying those known in the art and typically associated with biodegradable polymers alone. The invention requires that one of skill be able to make such a dosage form without empirical, undue and unpredictable trial and error experimentation; *i.e.*, the

skilled artisan must be able to recognize what structural features of the individual molecules comprising the ingredients in the dosage form will be compatible with one another such that the skilled artisan can take those structural features, identify other sets of compatible molecules, and create another useful finished (stable) dosage form. It is noted that the ability to "identify" sets of compatible molecules is not equivalent to "make and use" based on the principle above.

The scope of the invention is very broad, encompassing bioactive substances recited in the claims and specification of the instant application. However, there are only a few imprecisely described embodiments noted in the application, none of which explains how hydroxynaphthoates along with biodegradable polymers confer stability and control of drug release. Mechanism of the biodegradable polymers action in determining sustained release is well known to the artisan. The specification correctly teaches that pK_a of the hydroxynaphthoates likely plays a role, when it interacts with polymer, but does not adequately define that role. Further, the specification lacks suitable discussion of how the hydroxynaphthoate structural features drive the magnitude of the pK_a and how that impacts the presumed ionic interaction with the biodegradable polymer. Accordingly, the skilled artisan cannot make the broad scope of the invention as claimed.

The state of the art in pharmaceutical dosage formulation is well developed in terms of breadth of knowledge, and in terms of methods for assessing stability of finished dosage formulations. While there is an element of codified science to the art, the "breadth of knowledge" is actually a very large set of examples that have been well characterized by highly developed analytical techniques. Structural features of the

molecules comprising the finished dosage form notwithstanding, environmental factors, variable impurity profiles and the passage of time make dosage form stability prediction impossible without empirical data, and no artisan (skilled or otherwise) is expert in every type of compound or analytical technique.

Thus, the instant specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to employ the invention in a manner that is commensurate in scope with these claims (see MPEP § 2164.08). Accordingly, it would not be possible, even for one skilled in the art, to make and use the invention as claimed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 26, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by El-Naggar, *et al.*

The claims are directed to non-specific peptides and their hydroxynaphthoate derivatives. El-Naggar *et al.* teaches the syntheses of several examples of such compounds (see entire reference, especially Table 1).

Therefore, the claimed invention is anticipated by El-Nagger *et al.*

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 17 - 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaffe (4,272,398).

The claims are directed to production of a solid controlled release dosage form comprising a biologically active substance, excipients and a biodegradable polymer. The process involves dissolution of the ingredients in organic solvent, followed by treatment with an aqueous solution.

Jaffe teaches a micro-encapsulation process that yields a solid dosage form wherein the active ingredient and other formulation components are uniformly dispersed in a biodegradable polymer. The process comprises dissolving the formulation components and biodegradable polymer in a suitable organic solvent, then dispersing the resulting solution in aqueous medium. After evaporation of the organic solvent, the resulting solid mass can be formed into a capsule or tablet. Particle size and plasticity of the solid mass are controllable, thus release of the active ingredient from the biodegradable polymer matrix is controllable.

Thus, the claimed invention is prima facie obvious of Jaffe

Application Status and Examiner Contact Information

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey S. Eberhard, Ph.D. whose telephone number is (571) 270-3289. The examiner can normally be reached from 7:30 am to 5:00 pm EDT. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey S. Eberhard, Ph.D.
Patent Examiner
Art Unit 1609

JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER